

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application.

Listing of Claims:

Claim 1. (Currently Amended): A method of examining the physiological effect of a compound on a mammalian prostate cancer cell ~~wherein~~ in a cell, wherein said prostate cancer cell expresses an exogenous wild type androgen receptor polynucleotide that encodes an androgen receptor polypeptide or an androgen receptor polypeptide variant, ~~said cell further comprising an abnormal level of mRNA that encodes said androgen receptor polypeptide or, said androgen receptor polypeptide variant when compared to the level of mRNA that encodes said androgen receptor polypeptide or said androgen receptor polypeptide variant in a normal prostate cell;~~ such that the total levels of mRNA in the cell that encode said androgen receptor polypeptide or said androgen receptor polypeptide variant, or the total protein levels of said androgen receptor polypeptide or said androgen receptor polypeptide variant, are at least two-fold higher than the endogenous level of androgen receptor, mRNA or polypeptide in a hormone-sensitive prostate cancer cell, said method comprising:

(a) ~~determining that said abnormal level of mRNA in said prostate cancer cell is at least two fold higher than the level of mRNA in said normal prostate cell;~~

(b) (a) contacting a compound to be tested with said prostate cancer cell expressing exogenous wild type androgen receptor polynucleotide to provide a treated prostate cancer cell; and

(c) (b) examining comparing one or more physiological characteristics of said treated prostate cancer cell with the same one or more characteristics of a control prostate cancer cell to which said compound has not been administered, wherein a difference in the one or more characteristics indicates that said compound has a physiological effect on the treated prostate cancer cell,

wherein the growth of said mammalian prostate cancer cell is androgen-independent and

wherein said compound decreases the biological function of androgen receptors by decreasing androgen receptor DNA levels, androgen receptor mRNA levels, or androgen receptor protein levels, and

wherein said compound inhibits the growth of hormone-refractory prostate cancer cells.

Claims 2.-4. (Canceled)

Claim 5. (Original): A method of examining the physiological effect of a compound on a selected mammalian cancer cell wherein said cancer cell expresses an exogenous wild type polynucleotide that encodes a protein or polypeptide of interest, said cell further comprising an abnormal level of mRNA that encodes said protein or polypeptide of interest when compared to the level of mRNA that encodes said protein or polypeptide of interest in said normal selected cell, said method comprising:

- (a) determining that said abnormal level of mRNA in said selected cancer cell is at least two fold higher than the level of mRNA in said normal selected cell;
- (b) contacting a compound to be tested with said selected cancer cell to provide a treated cancer cell; and
- (c) examining one or more physiological characteristics of said treated cancer cell.

Claim 6. (Original): A method of examining the physiological effect of a compound on a selected mammalian cancer cell wherein said selected cancer cell expresses an exogenous wild type polynucleotide that encodes an abnormal level of protein or polypeptide of interest when compared to the level of said protein or polypeptide of interest encoded by a normal selected cell, said method comprising:

- (a) determining that said abnormal level of said protein or polypeptide of interest is at least two fold higher than the level of said protein or polypeptide of interest in said normal selected cell;

- (b) contacting a compound to be tested with said selected cancer cell to provide a treated cancer cell; and
- (c) examining one or more physiological characteristics of said treated cancer cell.

Claim 7. (Original): A method of examining the physiological effect of a compound on a selected mammalian cancer cell according to claim 5 which includes the additional steps of:

- (a) providing a mammalian cancer cell which is the same as said selected cancer cell and which is not contacted with said compound to thereby provide a control cancer cell; examining said one or more physiological characteristics of said control cancer cell; and comparing said one or more characteristics of said control cancer cell with said one or more characteristics of said treated cancer cell.

Claim 8. (Original): A method of examining the physiological effect of a compound on a selected mammalian cancer cell according to claim 6 which includes the additional steps of:

- (a) providing a mammalian cancer cell which is the same as said selected cancer cell and which is not contacted with said compound to thereby provide a control cancer cell; examining said one or more physiological characteristics of said control cancer cell; and comparing said one or more characteristics of said control cancer cell with said one or more characteristics of said treated cancer cell.

Claim 9. (Original): A method of examining the physiological effect of a compound on a selected mammalian cancer cell according to claim 5 wherein said selected mammalian cell is selected from the group consisting of breast cancer cells, ovarian cancer cells and prostate cancer cells.

Claim 10. (Original): A method of inhibiting the growth of hormone refractory prostate cancer cells wherein said cells comprise androgen receptors that exhibit biological function, said method comprising the step of decreasing the biological function of said androgen receptors.

Claim 11. (Original): A method of inhibiting the growth of hormone refractory prostate cancer cells according to claim 10 wherein said step of decreasing the biological function of said androgen receptors comprises affecting the androgen receptor DNA levels, androgen mRNA levels, or androgen protein levels.

Claim 12. (Original): A method of inhibiting the growth of hormone refractory prostate cancer cells according to claim 11 wherein the androgen receptor protein level is decreased through modulation of signal transduction pathways such as targeting EGF receptors that crosstalk to the androgen receptor.

Claim 13. (Original): A method of inhibiting the growth of hormone refractory prostate cancer cells according to claim 11 wherein the androgen receptor protein level is decreased by the induction of cellular degradation pathways.

Claim 14. (Original): A method of inhibiting the growth of hormone refractory prostate cancer cells according to claim 11 wherein the androgen receptor protein level is decreased by dissociating the androgen receptor from heat shock proteins that maintain the androgen receptor integrity

Claim 15. (Original): A method of inhibiting the growth of hormone refractory prostate cancer cells according to claim 11 wherein the androgen receptor protein level is decreased using androgen receptor antisense or mRNA knockdown technology.

Claim 16. (Original): A method of inhibiting the growth of hormone refractory prostate cancer cells according to claim 11 wherein the androgen receptor protein is decreased by modifying the polynucleotide or polypeptide sequence of the androgen receptor or by posttranslational modifications of the androgen receptor selected from the group consisting of phosphorylation, acetylation, ubiquitination, and sumolation.

Claim 17. (Original): A method for determining if a selected prostate cancer cell is hormone sensitive or has become hormone refractory, said method comprising the steps of:

- (a) determining the level of mRNA in said selected cell that encodes the androgen receptor polypeptide or androgen receptor polypeptide variant;
- (b) determining the level of mRNA in a hormone sensitive selected prostate cancer cell;
- (c) comparing the level of mRNA determined in step (a) to the level of mRNA determined in step (b); and
- (d) determining that the selected prostate cancer cell is hormone sensitive or has become hormone refractory if the level of mRNA determined in step (a) is at least two fold higher than the level of mRNA determined in step (b).

Claim 18. (Original): A method for determining if a selected prostate cancer cell is hormone sensitive or has become hormone refractory, said method comprising the steps of:

- (a) determining the level of androgen receptor polypeptide or the level of androgen receptor polypeptide variant in said selected cell;
- (b) determining the level of androgen receptor polypeptide or the level of androgen receptor polypeptide variant in a hormone sensitive selected prostate cancer cell;
- (c) comparing the level of androgen-receptor polypeptide or the level of androgen receptor polypeptide variant determined in step (a) to the level of androgen receptor polypeptide or the level of androgen receptor polypeptide variant determined in step (b) and
- (d) determining that the selected prostate cancer cell is hormone sensitive or has become hormone refractory if the level of androgen receptor polypeptide or the level of androgen receptor

polypeptide variant determined in step (a) is at least two fold higher than the level of androgen receptor polypeptide or the level of androgen receptor polypeptide variant determined in step (b).

Claim 19. (Previously Presented): A method of examining the physiological effect of a compound on a selected mammalian cancer cell according to claim 6 wherein said selected mammalian cell is selected from the group consisting of breast cancer cells, ovarian cancer cells and prostate cancer cells.

Claim 20. (New): The method of claim 1, wherein said compound modulates signal transduction pathways such as targeting EGF receptors that crosstalk to the androgen receptor, thereby decreasing androgen receptor protein levels.

Claim 21. (New): The method of claim 1, wherein said compound induces cellular degradation pathways.

Claim 22. (New): The method of claim 1, wherein said compound dissociates the androgen receptor from heat shock proteins that maintain the androgen receptor integrity.

Claim 23. (New): The method of claim 1, wherein said compound is an androgen receptor antisense mRNA molecule.

Claim 24. (New): The method of claim 1, wherein the total levels of mRNA in the mammalian prostate cancer cell that encode said androgen receptor polypeptide or said androgen receptor polypeptide variant, or the total protein levels of said androgen receptor polypeptide or said androgen receptor polypeptide variant, are at most five-fold higher than the endogenous level of androgen receptor, mRNA or polypeptide in a hormone-sensitive prostate cancer cell.